

PATENT COOPERATION TREATY

08/16/04 H/V

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

PCT

To:

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SUISSE

EINGEGANGEN 9 Jan. 2004

WRITTEN OPINION
(PCT Rule 66)Date of mailing
(day/month/year)

15.01.2004

Applicant's or agent's file reference
E1105-WO

REPLY DUE

within 3 month(s)
from the above date of mailingInternational application No.
PCT/EP 02/04153International filing date (day/month/year)
15.04.2002Priority date (day/month/year)
08.03.2002International Patent Classification (IPC) or both national classification and IPC
G01N33/58

Termin:

15.4.04

Applicant
EIDGENÖSSISCHE TECHNISCHE HOCHSCHULE LIBRARIES...Eintrag in
Fristenliste
durch:

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- This written opinion is the first drawn up by this International Preliminary Examining Authority.
- This opinion contains indications relating to the following items:
 - ☒ Basis of the opinion
 - ☐ Priority
 - ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
 - ☐ Lack of unity of invention
 - ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
 - ☐ Certain documents cited
 - ☐ Certain defects in the international application
 - ☐ Certain observations on the international application
- The applicant is hereby invited to reply to this opinion.

When? See the time limit indicated above. The applicant may, before the expiration of that time limit, request this Authority to grant an extension, see Rule 66.2(c).

How? By submitting a written reply, accompanied, where appropriate, by amendments, according to Rule 66.3. For the form and the language of the amendments, see Rules 66.8 and 66.9.

Also: For an additional opportunity to submit amendments, see Rule 66.4.
For the examiner's obligation to consider amendments and/or arguments, see Rule 66.4 bis.
For an informal communication with the examiner, see Rule 66.6.

If no reply is filed, the international preliminary examination report will be established on the basis of this opinion.
- The final date by which the international preliminary examination report must be established according to Rule 69.2 is: 08.07.2004

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WRITTEN OPINIONInternational application No. **PCT/EP 02/04153****I. Basis of the opinion**

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this opinion as "originally filed"*):

Description, Pages

1-5, 7-38 as originally filed
 6, 6a, 6b received on 09.08.2003 with letter of 07.08.2003

Claims, Numbers

1-32 received on 09.08.2003 with letter of 07.08.2003

Drawings, Sheets

1/10-10/10 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
☐ the language of publication of the international application (under Rule 48.3(b)).
☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
☐ filed together with the international application in computer readable form.
☐ furnished subsequently to this Authority in written form.
☐ furnished subsequently to this Authority in computer readable form.
☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
☐ the claims, Nos.:
☐ the drawings, sheets:

5. ☐ This opinion has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

6. Additional observations, if necessary:

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V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**1. Statement**

Novelty (N)	Claims	1-12
Inventive step (IS)	Claims	13-7, 19-24, 26-32
Industrial applicability (IA)	Claims	

2. Citations and explanations**see separate sheet**

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Re Item V**Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. The claims filed with the letter dated 07.08.2003 introduce subject-matter which extends beyond the content of the application as originally filed. The amendments concerned are the following:
 - (i) Claim 1 refers to compounds capable of building a "stable combination reaction product". The only explicit reference to a stable combination of self-assembly moieties can be found on page 15, paragraph 1, of the specification as originally filed, referring to heterodimerisation of DNA codes. No reference to stable combinations of other self-assembly moieties, e.g. such as defined in present claim 3, can be found in the application as originally filed.
An analogous argumentation also apply to claims 9 and 19.
This objection appears to be of particular relevance in view of the argument presented by the applicant in the letter of reply, dated 07.08.2003, page 1, last paragraph.
 - (ii) Claim 4 refers to a chemical compound, comprising at least one chemical group that is capable of forming a covalent bond with at least one respective chemical group of a similar chemical compound.
Support for a general reference to covalent coupling of two compounds according to claims 1-3 can be found, e.g., in figure 8, and on page 13, last paragraph of the specification as originally filed. However, the specification as originally filed does not contain a basis for a compound having "at least one chemical group", i.e. one or more than one chemical group for forming a covalent bond.
 - (iii) Claim 5 refers to a chemical compound characterised in that the oligonucleotide (b) is "covalently and directly linked" to chemical moiety (p). The explicit reference to a covalent and direct link implies that other possibilities of linkage will also have to be considered. The specification as originally filed does not disclose details about the mode of linkage of the chemical moiety (p) to oligonucleotide (b).

Therefore, claims 1, 4, 5, 9 and 19 do not meet the requirements of Article 19(2)

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2. Novelty

- 2.1 Claims 1-12 do not appear to be novel within the meaning of Article 33(2) PCT. Document DE-A-196 19 373 (D1) discloses libraries of compounds comprising an oligonucleotide part and a binding compound, e.g. a peptidic part, connected via a linking part. Individual molecules can assemble via their nucleic acid part into trimeric structures, thereby assembling the peptidic binding parts to form a binding domain for a substrate (see figure 1). Peptides with different properties from can be assembled and can form a multitude of different combinations compared to individually synthesised peptides (col. 3, lines 21-52). The assembled binding partners can be covalently cross-linked in order to obtain a binding entity for the target molecule (e.g. col. 4, lines 33-36).

Documents WO-0023458 (D2, see passages cited in the international search report) and US-A-5 573 905 (D3, abstract) also refer to oligonucleotide tagged libraries of chemical compounds.

Claims 1-12 refer to chemical compounds, and libraries of chemical compounds, respectively, which are characterised by a binding compound and a self-assembly moiety, e.g. an oligonucleotide part. The oligonucleotide is characterised as comprising a self-assembly sequence and a tag ("coding sequence") identifying the binding entity linked to the oligonucleotide. However, the terms "self-assembly sequence" and "coding" relate to the use of said sequences, but do not distinguish the oligonucleotides of the present claims from the oligonucleotides described in D1-D3. Every nucleic acid sequence can function as a self-assembly sequence by choosing an appropriate complementary sequence present in another molecule. The same is true for a coding tag sequence. The fact that said sequence is used for identifying a chemical entity linked thereto does not teach anything about the sequence itself. Moreover, D2 explicitly refers to nucleic acid tags having different hybridisation sequences (page 4, lines 5-7). The oligonucleotides disclosed in D2 are long enough to provide for a "self-assembly sequence" and a "coding" sequence, i.e. they are "capable" (claim 1) of performing the tasks of the oligonucleotides of claim 1. Claims 1-12 are directed to compounds as such and without any further definition, e.g. with respect to the presence of complementary self-assembly sequences in a library of compounds, the only characterising technical features of said compounds are a chemical binding moiety and an oligonucleotide part, such as present in compounds disclosed in D1-D3. Therefore claims 1-12 lack novelty (Article 33(2) PCT). The arguments of the applicant referring to documents D1-D3, and in particular

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the concluding paragraph of the letter dated 07.08.2003, pertain to the use of the compounds in the context of a self-assembling library, but less to the properties of the isolated compounds. Said arguments are thus not relevant for the question of novelty of present claims 1-12.

3. Inventive step**3.1 Claim 13 cannot be considered as being inventive within the meaning of Article 33(3) PCT.**

Claim 13 refers to a library of compounds wherein combinations of chemical binding moieties are obtained by interaction of self-assembly sequences, i.e. in contrast to claims 9-12, claim 13 actually defines that at least two complementary self assembly sequences have to be present in the library of compounds in order to obtain combinations of binding moieties.

The subject-matter of claim 13 differs from the teaching of D1, which is considered to represent the most relevant state of the art, in that the molecules constituting the complexes of binding moieties comprise a coding sequence identifying the chemical moiety bound to the oligonucleotide.

The technical problem underlying claim 13 may therefore be seen in providing means for identifying the chemical binding moiety included in multimeric complexes thereof.

Tagging chemical moieties which are capable of binding to a target molecule with an oligonucleotide in order to identify said moieties is well known in the art (see D2 and D3). It would therefore appear to be obvious for a skilled artisan to include a tagging sequence in the oligonucleotides disclosed in D1 in order to arrive at a solution to the above-stated problem.

Claims 14-17 appear to relate to standard embodiments in the art of coupling a chemical moiety to an oligonucleotide.

Claims 13-17 therefore do not appear to meet the requirements of Article 33(3) PCT.

3.2 Claim 18 appears to meet the requirements of Article 33(3) PCT. The use of oligonucleotides having therein-defined sequence of self-assembly sequences, spacer regions and coding sequences in one library is neither disclosed nor rendered obvious in the state of the art.**3.3 An analogous argumentation as put forward under item 3.1 appears to apply for the subject-matter of independent claims 19, dependent claims 20 and 21, and**

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independent claim 22, referring to a method of biopanning using the compounds of claims 1-8 or the library of claims 9-18, since D1 refers to identifying of ligands for target molecules (e.g. col. 1, lines 58-63).

Claims 19-22 thus do not appear to meet the requirements of Article 33(3) PCT.

- 3.4 Dependent claim 23, 24, and 26-32 do also not appear to meet the requirements of Article 33(3) PCT in view of the arguments put forward under item 3.1. Including a sequence "coding" for a chemical moiety cannot be considered as being inventive within the meaning of Article 33(3) PCT in view of documents D1-D3. Furthermore, identification of tags using PCR or selection of binding moieties onto a solid support are well known in the art (see for example D2, page 15, line 27 et seq., D3, col. 3, line 22 - col. 4, line 2).

- 3.5 Claim 25 meets the requirements of Article 33(3) PCT for reasons put forward under item 3.2 above.